REMARKS

Applicants have now had an opportunity to carefully consider the Examiner's comments set forth in the Office Action of July 29, 2004.

Reconsideration of the Application is requested.

STATEMENT OF SUBSTANCE OF INTERVIEW

Applicants wish to thank the Examiner for the courtesy of a telephone interview held on November 4, 2004, and the helpful suggestions made by the Examiner. The interview included a discussion of a set of proposed claims and amendments to the specification. New claim 184 was discussed and a general agreement was reached on acceptable language, which is reflected in the present amendment.

The addition of the words "or repeats" to clarify the language "comprising two to fifty units" at various points throughout the specification was also discussed. The applicants pointed out that the Examiner's reading of "units" as "amino acid residues" was not consistent with the specification which shows SEQ. ID No. 5 as having fifteen amino acid residues. Accordingly, the upper limit of 50 units, which is substantially higher than the number of residues, implies repeats rather than amino acid residues, i.e., that a polypeptide contains more than one string of SEQ ID No. 5 in its length. Thus, for example, a polypeptide comprising 50 units of Seq. ID. No. 5 would be 750 residues in length.

The Examiner also asked whether the specification identified five of the amino acids in Seq. ID No. 5 which were considered to be key. Applicants noted that new claim 187 identifies amino acids 1-6 of SEQ. ID No. 5. This finds support in paragraphs [0106] ((page 34, lines 35-43), and Example 7 at paragraphs [0214] and [0215] (page 55, line 38-page 56, line 18). Polypeptide 22-36, referred to in this example corresponds to amino acid residues 22-36 of SEQ. ID No. 1, as follows:

Lys Gly Asn Lys His Pro Ile Asn Ser **Glu Trp Gln Thr Asp Asn**

The last six residues correspond to the first six residues of SEQ ID No. 5.

FIGURE 11 of the application shows that this polypeptide has an inhibitory effect on PC-3 (human tumor cells) cells in 72 hours.

The Examiner also requested that Applicant's response provide support, in the examples, for a polypeptide having at least 50% (or another specified percentage) of its amino acid sequence identical to that of SEQ. ID NO. 5.

Status of Application

Claims 184-223 are pending in the application.

Claims 1-183 are canceled without prejudice.

New claims 184-223 are added.

The Office Action

The Examiner issued a restriction requirement. Applicants confirm their election of Group III, claims 1-3, 65-68, 71-76, 83-89, 157-168, and 175-183 (to the extent that the claims read on SEQ ID No: 5 and analogs of SEQ ID NO: 5, and pharmaceutical compositions comprising SEQ ID NO: 5 and analogs of SEQ ID NO: 5). It is submitted that new claims, with the exception of claims 197, 206, 211, 213, 218, 221, and 223, conform to Group III.

Applicants respectfully request rejoinder of claims 197, 206, 211, 213, 218, 221, and 223, should an allowable product claim be found.

Claims 1-3, 65-68, 73-76, 83-89, 157-168, and 175-183 were rejected under 35 USC 102(b) as being anticipated by U.S. Patent No. 5,427,011 to Sheth.

Claims 2, 3, 84, and 86 were rejected under 35 USC 102(b) as being anticipated by U.S. Patent No. 5, 994, 298 to Tsai as evidenced by U.S. Patent No. 6,319,894 to Tracey.

Claims 2 and 3 were rejected under 35 USC 102(b) as being anticipated by Nolet , et al, Biochimica Byophysica Acta 1089: 247-249, 1991 (Herein after Nolet).

Claims 2 and 3 were rejected under 35 USC 102(b) as being anticipated by Xuan, et al. DNA and Cell Biology 16: 627-638, 1997 (Herein after Xuan).

The Applicant would also like to bring to the Examiner's attention that receipt of the certified copies of the priority documents has not been acknowledged in the Office Action Summary dated 07/29/2004. These documents were filed on February 26, 2002. The Applicant would like to receive confirmation of their recordation at the Patent Office.

For the reasons outlined below, it is submitted that claims 184-223 are now in condition for allowance.

35 U.S.C. §112 rejections

Claims 2, 3, 65-68, 73-76, 83-89, 157-168, and 175-183 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner objected to use of phrases such as "two to fifty units of SEQ ID NO: 5," and the like. While not conceding to the Examiner's interpretation, Applicants' new claims avoid this phrase and others to which the Examiner objects. New claim 219 recites "at least two repetitions of the amino acid sequence defined in SEQ ID NO.:5" and thus encompasses a polypeptide with at least two complete fifteen residue portions (repetitions) identical to SEQ ID NO: 5.

Claims 65-68 were considered to be indefinite because it was unclear whether the claims were drawn to a polypeptide consisting of or comprising SEQ ID NO: 5. Applicants submit that the new claims meet the requirements of 35 U.S.C. §112, second paragraph, and request that the objection be withdrawn. In particular, Applicants have used "consisting of" and "comprising" rather than "set forth."

Claims 2, 3, 83-89, and 175-183 were objected to under 35 U.S.C. §112, first paragraph, for failing to comply with the written description. The Examiner asserted that the specification does not provide enablement for structural variants of SEQ ID NO: 5. The claims as now presented, do not refer to structural variants. Accordingly, it is requested that the objection be withdrawn.

With respect to the Examiner's rejection as to the disclosure lacking enablement and lacking adequate written description, examples or guidance towards variants, the Applicants respectfully submit that polypeptide 22-36, which is exemplified in Figure 11 and Example 7, is a variant of SEQ ID NO.:5. Polypeptide 22-36 corresponds to amino acids 22 to 36 of SEQ ID NO.:1 and overlaps SEQ ID NO.:5. In fact, polypeptide 22-36 and SEQ ID NO.:5 share six common amino acids (Glu-Trp-Gln-Thr-Asp-Asn). Thus, polypeptide 22-36 is an exemplified variation of SEQ ID NO.:5. In addition, at pages 10 to 12 and more particularly in SEQ ID NOS.:10 to 88 and SEQ ID NOS.:90 to 92, the Applicant has given several examples of alternatives to SEQ ID NO.:5.

SEQ ID NO.:5 and polypeptide 22-36 represent working embodiments of polypeptides of 64 amino acids long or less having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.: 5 capable of inhibiting the growth of a tumor cell and/or capable of inhibiting the growth of prostate adenocarcinoma. Polypeptides having the amino acids sequence defined in SEQ ID NOs.:10 to 88 or SEQ ID NOs.:90 to 92 are other examples of polypeptides of 64 amino acids long or less having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.: 5.

In addition, SEQ ID NO.:5 and polypeptide 22-36 are working embodiments which possess 40% or more of its amino acid sequence identical to the amino acid sequence defined in SEQ ID NO.:5. Polypeptide 22-36 possesses 6 amino acids out of 15 amino acids (i.e., 40%) which are identical to SEQ ID NO.:5. Polypeptides having the amino acids defined in SEQ ID NOs.:10 to 24, SEQ ID NOs.:59 to 73, SEQ ID NO.:89 and SEQ ID NOs.: 90 to 92 are other examples.

Higher percentages, such as those of new claims 190- 193 and 199-202, also find support. Applicants note that one skilled in the art recognizes that conservative replacement amino acids (as described at page 23; lines 32 to page 24, line 4 and page 24; lines 16 to 31, and Table 1) can be used where such changes do not substantially alter the overall biological activity of the polypeptide. At page 26; lines 6 to 13 (SEQ ID 89) the SEQ ID No. 5 polypeptide:

5 10 15

E W Q T D N C E T C T C Y E T

is modified to:

5 10 15

X_1 W Q X_2 D X_1 C X_1 X_2C X_2C $X_3X_1X_2$

Where X_1 is E, D, or N

X_2 is T or S

$X_3$is Y or F

Since there are nine amino acids which can be varied from the amino acid in SEQ ID 89 to another amino acid, the percent homology can be varied while retaining conservative substitutions. For example, the sequence

E W Q T D N C D S C S C F D S

has the first seven residues identical to SEQ ID. No. 5 but substitutions at 8, 9, 11, 13, 14, 15 and is thus 60% homologous (9aa out of 15aa), i.e., at least 50% identity. Adding an additional substitution at position 6 would yield an analog which is 53% homologous, i.e., at least 50% identity. With fewer substitutions, the percentage identity increases.

Therefore, the Applicant has described and enabled polypeptides "of 64 amino acids long or less having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.:5" and "having at least 40% (or at least 50%, etc.) of its amino acid sequence identical to the amino acid sequence defined in SEQ ID NO.:5" demonstrating biological activity (i.e., capable of inhibiting the growth of a tumor cell and/or capable of inhibiting the growth of prostate adenocarcinoma).

Claims 75, 88, 161-163, and 176-178 were objected to under 35 U.S.C. §112, first paragraph, for failing to comply with the written description. These claims were considered to be indefinite for use of the phrase taxol derivative. Applicants' new claims specify the taxol derivatives taxotere and taxane, as supported by the specification at page 6; line 21 and page 70; line 16. Accordingly, it is requested that the objection be withdrawn.

In light of the above, the Applicant respectfully submits that the specification provides written description and is enabling for polypeptides and pharmaceutical compositions of the present invention. Thus, the Applicant believes that new claims 184-223 overcome the Examiner's objections with respect to 35 U.S.C. §112.

The status of the new claims and exemplary support is summarized as follows:

Claim No.	**Support**
184	original claims 2 and 3, SEQ ID No.:10-88 and 90-92, page 34; line 42-43, page 55; line 38-page 56; line 18, page 56; line 35 of the description
185	original claims 2 and 3
186	original claim 1
187	page 34; lines 42-43 and page 55; line 38 to page 56; line 18 of the description
188	original claims 2 and 3
189	original claims 2 and 3

190	original claims 2 and 3
191	original claims 2 and 3
192	original claims 2 and 3, page 34; line 40 of the description
193	original claims 2 and 3
194	original claims 85 and 86 (and same as for claim 184)
195	original claim 177, page 6; line21 and page 70; line 16 of the description
196	original claim 180
197	original claims 55-56
198	original claims 2 and 3, SEQ ID No.:89
199	original claims 2 and 3
200	original claims 2 and 3
201	original claims 2 and 3, page 34; line 40 of the description
202	original claims 2 and 3
203	original claim 85, (and same as for claim 198)
204	original claim 177, page 6; line 21 and page 70, line 6 of the description
205	original claim 180
206	original claims 55-56 (and same as for claim 203)
207	original claims 67 and 68
208	original claims 158 and 159
209	original claims 161 and 163, page 6; line 21 and page 70; line 16 of the description
210	original claims 165 and 166
211	original claims 29 and 30
212	original claim 86, (and same as for claim 187)
213	original claims 55 and 56
214	original claims 67 and 68
215	original claims 158 and 159
216	original claims 161 and 163, page 6; line 21 and page 70; line 16 of the description
217	original claims 165 and 166
218	original claims 29-30

219	original claims 2 and 3, SEQ ID NO.: 90-92, page 29; line 36-39 of the description
220	original claims 85 and 86 (and same as for claim 219)
221	original claims 55-56
222	original claims 85 and 86 (and same as for claim 185)
223	original claims 55-56

Prior Art Rejections

New **claim 184** recites a polypeptide of from five to 64 amino acids that inhibits the growth of a tumor cell or inhibits the growth of prostatic adenocarcinoma, wherein at least five contiguous amino acids of said polypeptide are identical to five contiguous amino acids of SEQ ID NO: 5.

Support for new claim 184 is as defined above. More particularly, support for the expression "a polypeptide of from five to 64 amino acids long having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.:5" may be found in original claim 2, in the description at page 34, line 42-43, in Example 7 at page 55, line 38-page 56, line 18 and in SEQ ID NOS.:10-88 as well as in SEQ ID NOS.:90-92 which enumerate such polypeptides (see pages 27; line 17 to page 30; line 11). Support for the expression "tumor cells" may be found, for example, at page 56, line 35.

The references of record do not disclose or fairly suggest such a polypeptide. Sheth does not teach or suggest a polypeptide or pharmaceutical composition (comprising a polypeptide) of five to 64 amino acids long having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.:5. Rather, Sheth discloses an amino acid sequence which is ninety-four amino acid residues long. The present inventors have found a significantly shorter polypeptide has the capability of inhibiting the growth of a tumor cell and/or capable of inhibiting the growth of prostatic adenocarcinoma, reducing the length of the polypeptide which can used. This has significant advantages in the synthesis (manufacture) of the polypeptide as well as in formulating a pharmaceutical composition.

Tsai (the '298 patent) as evidenced by Tracey (the '894 patent) was said to teach polypeptides and pharmaceutical compositions comprising at least two

contiguous amino acids of SEQ ID NO.:5. Tsai, et al. discloses a method of inducing apoptosis in cancer cells by administering fetuin to the cancer cells. Tracey suggests that human fetuin has the amino acids Cys Thr at positions 248-249. However, Tsai does not teach or suggest a polypeptide of five to 64 amino acids long having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.:5, as presently claimed.

Therefore, the Applicants respectfully submit that new claims 184-197 are patentably distinct from the teachings of Tsai (evidenced by Tracey).

Nolet, et al. was said to disclose a polypeptide that has 81.4% sequence identity to SEQ ID NO.:5. However, Nolet's polypeptide is 114 amino acid long. As for the sequence of Sheth, this is much longer than the 64 residues presently claimed. Therefore, the Applicant respectfully submits that Nolet does not teach or suggest a polypeptide of five to 64 amino acids long having at least five contiguous amino acids identical to five contiguous amino acids of SEQ ID NO.:5".

In light of the above, the Applicant respectfully submits that new claims 184-197 are patentably distinct from the teachings of Nolet.

Xuan discloses a polypeptide of 114 amino acid long. As for Sheth, this is much longer than the 64 residues presently claimed. Therefore, the Applicant respectfully submits that Xuan does not teach or suggest a polypeptide of 64 amino acids long.

In light of the above, the Applicant respectfully submits that new claims 184-197 are patentably distinct from the teachings of Xuan.

Accordingly, it is submitted that claim 184, and claims 185-190, 212-213, and 222-223 dependent therefrom, distinguish patentably over the references of record.

New **claim 198** recites a polypeptide which inhibits the growth of a tumor cell, and/or inhibits the growth of prostatic adenocarcinoma. The polypeptide has at least 40% of its amino acid sequence identical to the amino acid sequence defined in SEQ ID NO.:5.

Support for the expression "at least 40% of its amino acid sequence identical to the amino acid sequence defined in SEQ ID NO.:5" may be found in the paragraph beginning at page 9, line 36. Moreover, SEQ ID NO.:89 shows a polypeptide of sequence X_1**WQ**X_2**D**X_1**C**X_1X_2**C**X_2**C**$X_3X_1X_2$ having therefore, 40% of its amino acids sequence (6 amino acids (in original) out of 15 amino acids) identical to

the amino acid sequence identified in SEQ ID NO.:5. SEQ ID NO.:89 uses conservative replacements for amino acids of an effective sequence, SEQ ID NO.:5.

The Examiner argues that Sheth teaches a polypeptide (HSPI) which comprises at least 50%, 70% or 90% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO.:5. However, Sheth discloses an amino acid sequence which is ninety-four amino acid residues long. Only fifteen of these residues are identical to the amino acid sequence identified in SEQ ID NO.:5. Therefore, Sheth shows a polypeptide having only about 16% (15 amino acids out of 94 amino acids) of its amino acid sequence identical to the amino acid sequence of SEQ ID NO.:5, i.e., significantly less than the 40% presently claimed.

Tsai, as evidenced by Tracey teaches a polypeptide (human fetuin) of which substantially less than the 40% amino acids claimed are identical to the amino acid sequence identified in SEQ ID NO.:5.

Nolet, et al. was said to disclose a polypeptide that has 81.4% sequence identity to SEQ ID NO.:5. However, Nolet's polypeptide is114 amino acid long. Only 11 amino acids out of 114 (9.6%) are identical to the amino acid sequence defined in SEQ ID NO.:5.

Xuan discloses a 114 residues long polypeptide of which13 amino acids out of 114 (11.4%) are identical to the amino acid sequence defined in SEQ ID NO.:5.

The references of record fail to disclose a polypeptide with at least 40% of its amino acid sequence identical to the amino acid sequence defined in SEQ ID NO.:5.

Accordingly, it is submitted that claim 198, and claims 199-206 dependent therefrom distinguish over the references of record.

New **claim 207** recites a pharmaceutical composition comprising a polypeptide consisting of the amino acid sequence defined in SEQ ID NO.:5 and a pharmaceutical carrier and/or anticancer drug.

The references of record do not disclose such a composition. In particular, neither Sheth, Tsai, Nolet, nor Xuan discloses a polypeptide consisting of the amino acid sequence defined in SEQ ID NO.:5 All of these references require much longer polypeptide chains. Tsai, Nolet, and Xuan all disclose lengthy polypeptides of which only a small portion overlaps a portion of SEQ ID No. 5. The present inventors have

found that a polypeptide which consists of the 15 residue fragment is effective in a pharmaceutical composition.

Accordingly, it is submitted that claim 207, and claims 208-211 dependent therefrom, distinguish patentably and unobviously over the references of record.

New **claim 214** recites a pharmaceutical composition comprising a polypeptide comprising SEQ ID NO.:5 provided that said polypeptide is not as defined in SEQ ID NO.:1 and at least one of an anticancer drug and a pharmaceutically acceptable carrier.

The references of record do not disclose such a composition. Sheth discloses a polypeptide according to SEQ ID NO.:1. The Tsai, Nolet and Xuan references do not disclose a pharmaceutical composition comprising a polypeptide comprising SEQ ID NO.:5.

New **claim 219** recites a polypeptide comprising at least two amino acid sequences identical to the fifteen amino acid sequence defined in SEQ ID NO.:5.

Support for new claim 219 is to be found in the specification in SEQ ID NOs.: 90 to 92 and at page 29, lines 36-39.

The references of record do not disclose such a polypeptide. Sheth discloses a single fifteen residue sequence of SEQ ID NO.:5 in a long chain polypeptide. Sheth does not identify the fifteen residues of SEQ ID NO.:5, or a selected portion of these residues, as being of particular significance. Nor does Sheth suggest including more than one of SEQ ID NO.:5 in a polypeptide chain. Tsai, Nolet, and Xuan make no suggestion of even one fifteen amino acid sequence as defined in SEQ ID NO.:5. Accordingly, it is submitted that claim 219 and claims 220-221 dependent therefrom, distinguish over the references of record.

In view of the Examiner's restriction requirement, the Applicant retains the right to present claims 4-64, 69-72, 77-82, 90-156, 169-174 as well as claims 1-3, 65-68, 73-76, 83-89, 157-168 and 175-183 with respect to SEQ ID NO.: 2, 3, 4, 6, 7 and SEQ ID NO.: 2, 3, 4, 6, 7 analogs in a divisional application.

CONCLUSION

For the reasons detailed above, it is submitted claims 184-223 are now in condition for allowance. An early allowance of these claims is respectfully requested.

In the event the Examiner considers further personal contact advantageous to the disposition of this case, she is hereby authorized to call Ann M. Skerry, at telephone number (216) 861-5582.

Respectfully submitted,

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